REMARKS

Claims 40-44 and 46-54 are pending in this application. An appendix with the pending claims is attached for the Examiner's convenience.

Support for amended claim 40 is found at least on page 25, lines 16-22.

Support for new claims 46-49 is found at least on page 26, lines 16-20 through page 27, lines 1-22.

Support for new claims 50-54 is found at least on page 11, lines 1-5.

Applicants acknowledge the reminder regarding inventorship.

Applicants note the Examiner has granted an effective filing date to the present application. Applicants submit that the present invention is not obvious or anticipated by the art published prior to the stated effective filing date, and therefore, submit it is not necessary to determine the effective filing date at this time. The comments which follow in no way are a commentary by applicants on whether the priority date should or should not be granted.

Rejection Under 35 U.S.C. § 102(b)

Claims 40 and 43 are rejected under 35 U.S.C. §102(b) as being anticipated by Sharan et al., (1997) Nature, 386:804-810.

The Office Action states that Sharan et al. use a two-hybrid screen to measure binding between RAD51 and BRCA2 proteins, and thus, anticipates the claimed invention.

The claims have been amended herein and now recite compositions including a physiologically acceptable carrier. As amended, the claims define a composition which is not taught, suggested or made obvious by Sharan et al. *In re King,* 231 USPQ 136; *Rohm & Haas Co. v. Crystal Chemical Co.*, 220 USPQ 289.

Sharan et al. disclose a yeast two-hybrid system as a means for demonstrating interactions between RAD51 and BRCA2 proteins. Sharan et al. does not teach or suggest

combining the nucleic acids encoding RAD51 and BRCA2 proteins with a physiological carrier.

Therefore, Sharan et al. does not disclose all of the claimed elements within its four corners as required to anticipate. Applicants, respectfully request the rejection be withdrawn.

Claims 40 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Sturzbecher et al., (1996) EMBO J., 15:1992-2002.

The Office Action states that Sturzbecher et al. show a binding assay between p53 and RAD51 proteins.

As stated above, the claims have been amended to recite compositions comprising a physiologically acceptable carrier. See specification, page 26, lines 16-21.

To anticipate a claim, a reference must teach "each and every element" of the claim. See *SSIH Equipment S.A.v. U.S. Inc. Int'l Trade Commission*, 218 USPQ 678, 688 (Fed. Cir. 1983). Applicants respectfully assert that Sturzbecher et al. do not teach or suggest compositions of nucleic acids encoding RAD51 and p53 proteins.

Sturzbecher et al. demonstrate *in vitro* and *in vivo* binding between RAD51 and p53 proteins, but make no suggestion that nucleic acids encoding RAD51 and p53 proteins can be combined *in vitro* or *in vivo*. Struzbecher et al. isolate RAD51 protein using *in vitro* transcription/translation from a commercially obtained plasmid. See Materials and Methods, page 2000. Purified p53 protein is obtained from *E. coli* cells transformed with a vector containing p53. Struzbecher et al. do not teach or suggest that nucleic acids encoding RAD51 and p53 proteins can be combined in a cell or in a test tube. Rather, the methods of Struzbecher et al. teach that RAD51 protein may be isolated using *in vitro* transcription/translation from a commercially available vector and that p53 proteins may be obtained from plasmid transformed *E. coli* cells. See Materials and Methods, page 2000.

In conclusion, Struzbecher et al. do not disclose compositions comprising nucleic acids encoding Rad51 and BRCA1. Accordingly, since each and every element is not present, the rejection under 35 U.S.C. § 102(b) is improper and should be withdrawn.

Claims 40 and 42 are rejected under 35 U.S.C. § 102(b) as being anticipated by Scully et al., (1997) Cell, 88:265-275.

The Office Action states that Scully et al.demonstrates binding between BRCA1 and Rad51 proteins.

As stated above, the claims have been amended to recite compositions comprising nucleic acids encoding RAD51 protein, BRCA1 protein and a physiologically acceptable carrier.

Scully et al. disclose methods for the construction of BRCA1 and Rad51 expression vectors, transient infection of cells with either BRCA1 or Rad51 vectors, methods for the expression of BRCA1 fusion proteins and methods for the detection of BRCA1 and Rad51 protein complexes in cell extracts. Scully et al. do not disclose methods where the nucleic acids encoding RAD51 and BRCA1 are combined *in vivo* or *in vitro*. Further, Scully et al. do not teach or suggest compositions comprising BRCA1, Rad51 and a physiological carrier.

Thus, Scully et al. does not disclose all of the claimed elements within its four corners as required to anticipate. Applicants respectfully request the rejection be withdrawn.

Rejection Under 35 U.S.C. § 103(a)

Claims 40 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Sturzbecher et al. in view of Scully et al. in view of Sharan et al.

The Office Action states that it would be obvious to a person of ordinary skill in the art to combine genes encoding RAD51, BRCA1, BRCA2 and p53 proteins because the

combination of references show such a combination would be useful to assay binding of RAD51 to BRCA1, BRCA2 and p53.

As amended, claim 40 is drawn to a composition comprising nucleic acids encoding a RAD51 protein, a tumor suppressor gene, and a physiological carrier.

Scully et al. disclose methods for the construction of a BRCA1 expression vector, a Rad51 expression vector, methods for transiently infecting cells with either BRCA1 or Rad51, methods for the expression of BRCA1 fusion proteins and methods for the detection of BRCA1 and RAD51 protein complexes in cell extracts. Scully et al. do not teach methods where the nucleic acids encoding RAD51 and BRCA1 proteins are combined *in vivo* or *in vitro*.

Struzbecher et al. disclose isolation of RAD51 protein using *in vitro* transcription/translation from a commercially available plasmid containing a Rad51 cDNA insert. Struzbecher et al. disclose isolation of purified p53 protein from *E. coli* cells transformed with a p53 plasmid. The methods of Struzbecher do not teach or suggest that nucleic acids encoding RAD51 and p53 can be combined *in vivo* or *in vitro* in the same cell or test tube.

Sharan et al. describe a yeast two-hybrid screen demonstrating protein-protein interactions between Rad51 and BRCA2. Sharan et al. do not describe experiments in which compositions comprising the nucleic acids encoding RAD51 protein, BRCA2 protein and a carrier are combined *in vitro* or in vivo

The requirements for establishing a *prima facie* case of obviousness are: i) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; ii) there must be a reasonable expectation of success; and iii) the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on

applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) M.P.E.P. §2143.

In the present case, the cited art, either alone or in combination, does not disclose each of the claimed elements. Scully, Sharan, and Struzbecher do not disclose a composition comprising a nucleic acid encoding RAD51 protein, a nucleic acid comprising a tumor suppressor gene, and a physiological carrier. Therefore, the requirement of teaching or suggesting all the claim elements has not been met.

Moving to the issue of whether the disclosures suggest that the elements be combined, Applicants respectfully submit that the elements are not disclosed, therefore, there can be no suggestion that they be combined to arrive at the present invention.

Lastly, there is no reasonable expectation of success at arriving at the present invention by combining Scully, Struzbecher and Sharan. Scully, Struzbecher and Sharan do not teach or suggest compositions comprising nucleic acids encoding RAD51 protein, a tumor suppressor gene, and a carrier. Therefore, the skilled artisan would not be led to arrive at the present invention without undue experimentation from the disclosures of Scully, Sharan and Struzbecher.

In view of these remarks, Applicants respectfully submit that the references either alone or in combination do not support a conclusion of obviousness and respectfully request the rejection be withdrawn.

Claim 44 is rejected under 35 U.S.C. §103(a) as being unpatentable over Sturzbecher et al. in view of Scully et al. in view of Sharan et al. Applicants respectfully disagree.

Applicants respectfully submit that the arguments put forth above in response to the Section § 103(a) rejection of Claim 40 apply in traversing the rejection of Claim 44. There is no teaching or suggestion in Struzbecher, Scully, or Sharan that a composition comprising nucleic acids encoding RAD51, BRCA1, BRCA2, p53 and a carrier may be combined *in vivo* or *in vitro*.

Struzbecher et al. disclose binding interactions between RAD51 and p53 proteins in which the RAD51 protein is transcribed/translated *in vitro* and the p53 protein is purified from cell extracts of transformed E. coli cells. Scully et al. disclose binding interactions between RAD51 and BRCA1 in which cells are transiently infected with either an expression vector encoding Rad51 or BRCA1. Sharan et al. may be relevant to a composition comprising a nucleic acid encoding RAD 51 protein and a nucleic acid encoding BRCA2, but Sharan does not cure any of the defects with regard to a carrier or to a composition comprising nucleic acids encoding RAD51, BRCA1, BRCA2 and p53.

Therefore, Applicants respectfully submit that the references, either alone or combination, do not support a conclusion of obviousness and respectfully request the rejection be withdrawn.

Applicants submit the claims are now in condition for allowance and an early notification of such is respectfully solicited. If after review, the Examiner feels there are further unresolved issues, the Examiner is invited to call the undersigned at (415) 781-1989.

The Commissioner is authorized to charge any additional fees which may be required or credit any overpayment to Deposit Account No. 06-1300 (our Order No. A65680-4/RFT/RMS/DAV/RMK).

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Respectfully submitted,

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APPENDIX OF PENDING CLAIMS

40. (Amended) A composition comprising:
a) nucleic acid encoding a Rad51 protein; [and]
b) nucleic acid encoding a tumor suppressor protein[.]; and
c) a physiological carrier.

41. (Amended) A composition according to claim [38] 40 wherein said tumor suppressor protein is p53.

42. (Amended) A composition according to claim [38] 40 wherein said tumor suppressor protein is BRCA1.

43. (Amended) A composition according to claim [38] 40 wherein said tumor suppressor protein is BRCA2.

44. (Amended) A composition according to claim [38] 40 comprising:
a) nucleic acid encoding a Rad51 protein;
b) nucleic acid encoding a BRCA1 protein;
c) nucleic acid encoding a BRCA2 protein; and
d) nucleic acid encoding a p53 protein.

46. A human cell comprising a recombinant nucleic acid encoding a RAD51 protein and a recombinant nucleic acid encoding a tumor suppressor protein.

47. A human cell according to claim 46 wherein said tumor suppressor protein is BRCA1.

48. A human cell according to claim 46 wherein said tumor suppressor protein is BRCA2.

49. A human cell according to claim 46 comprising:
a) a recombinant nucleic acid encoding a RAD51 protein;
b) a recombinant nucleic acid encoding a BRCA1 protein;
c) a recombinant nucleic acid encoding a BRCA2 protein; and
d)a recombinant nucleic acid encoding a p53 protein.

50. A human cell according to claim 46 wherein said human cell is a breast tissue cell.

51. A human cell according to claim 46 wherein said human cell is a cancerous breast tissue cell.

52. A human cell according to claim 46 wherein said human cell is a cancerous cell.

53. A human cell according claim 46 wherein said human cell is in a cell culture.

54. A human cell according claim 46 wherein said human cell is isolated.